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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/586,242      06/02/2000      James McKim      28341/6281A      6518

7590      12/13/2001

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EXAMINER

OZGA, BRETT T

ART UNIT

PAPER NUMBER

1651

7

DATE MAILED: 12/13/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.  
**09/586,242**

Applicant(s)  
**McKim et al.**

Examiner  
**Ozga, Brett**

Art Unit  
**1651**

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on Oct 1, 2001.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-42 is/are pending in the application.
- 4a) Of the above, claim(s) 39-42 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-38 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claims \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some\* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \*See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

## Attachment(s)

- 15) ☐ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_
- 18) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

The response filed 10/01/01 has been received and considered.

The text of those sections of Title 35, US Code, not included in this action can be found in a previous office Action.

Claims 1-42 are pending. Claims 1-38 are examined on the merits.

### ***Election/Restrictions***

This application contains claims 39-42, drawn to an invention nonelected with traverse in Paper No. 8. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

### ***Claim Rejections - 35 USC § 103***

Applicant's arguments have been considered but are not deemed persuasive. Note that contrary to applicant's argument on p.6 of Paper No. 8, the individual of skill in the art would have a reasonable expectation of success of achieving the desired result in that the cited references do not teach away from such a result in all instances.

Claims 1-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kangas et al. (Med Biol, 62:338-343, 1984) in view of Redick et al. (J. Biol. Chem, 257:15200-3) and Connors et al. (Biochem Pharmacol 24:2217-24, 1975).

The instant application's first independent claim is a method of predicting the in vivo cytotoxicity of a chemical compound comprising: culturing cells in a culture medium that comprises a plurality of concentrations of said chemical compound; measuring three indicators of cell health; and predicting a toxic concentration of said chemical compound from the measurements. Dependent claims further limit by choosing the indicators from those for cellular replication, membrane integrity, mortality, mitochondrial function, and intracellular energy balance. They also limit by using a concentration range from 0-300 micromolar.

Dependent claims further limit by monitoring cellular replication with an assay that measures H-thymidine incorporation and mitochondrial function with an ATP assay. They further limit by choosing the cells from liver cell lines and being used to treat cancer.

Kangas and Redick teach ATP assays, MTT assays, Alamar Blue assays and Rhodamine 123 assays, all of which are well known in the art.

Kangas et al. teach a method of predicting the cytotoxicity of a chemical compound comprising: culturing cells in a culture medium (see abstract) and measuring cell mortality, cellular replication, mitochondrial function with an ATP assay and intracellular energy balance. (See paragraph 1 of introduction) Kangas et al. also teach

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the treatment of cancer (see abstract). Kangas does not teach in vivo or choosing the cells from liver cells lines.

Redick teaches choosing the cells to be used in predicting the cytotoxicity of chemical compounds from liver cell lines (See methods) and Connors et al. teach in vivo methods of screening for anti-cancer agents and predicting the cytotoxicity of chemical compounds. (See "anti-tumour selectivity" section)

One of ordinary skill in the art would be motivated to modify the teaching of Kangas et al. by the addition of liver cell lines as taught by Redick and in vivo as taught by Connors based on the common cytotoxic agents (i. e. antitumor agents) found in each of the references

It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to modify the teaching of Kangas et al. by the addition of liver cell lines as taught by Redick and in vivo as taught by Connors to attain the advantages of such as disclosed by Connors, namely to facilitate the use of the techniques in real world pharmaceutical compositions instead of merely in vitro testing.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brett T Ozga whose telephone number is 7033050634. The examiner can normally be reached on M-F 0530-1500, 2nd Wednesday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 7033084743. The fax phone numbers